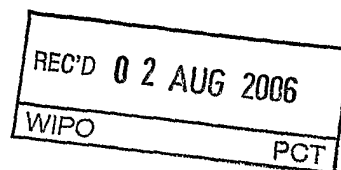


PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 93616-3	<div style="display: flex; justify-content: space-between;"> FOR FURTHER ACTION See Form PCT/IPEA/416 </div>	
International application No. PCT/CA2005/000423	International filing date (<i>day/month/year</i>) 22 March 2005 (22-03-2005)	Priority date (<i>day/month/year</i>) 26 March 2004 (26-03-2004)
International Patent Classification (IPC) or national classification and IPC IPC: C07F 9/40 (2006.01), C07F 7/02 (2006.01), C07D 317/60 (2006.01), C07D 307/54 (2006.01), C07D 213/40 (2006.01), C07C 317/32 (2006.01) (more IPCs on the last page)		
Applicant HSC RESEARCH AND DEVELOPMENT LIMITED PARTNERSHIP ET AL		
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>8</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. 1 and the Supplemental Box. b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions). 4. This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input checked="" type="checkbox"/> Box No. VII Certain defects in the international application <input checked="" type="checkbox"/> Box No. VIII Certain observations on the international application		
Date of submission of the demand 20 January 2006 (20-01-2006)	Date of completion of this report 26 July 2006 (26-07-2006)	
Name and mailing address of the IPEA/CA Canadian Intellectual Property Office Place du Portage I, C114 - 1st Floor, Box PCT 50 Victoria Street Gatineau, Quebec K1A 0C9 Facsimile No.: 001(819)953-2476	Authorized officer <div style="text-align: right;">Wesley Sharman (819) 934-2326</div>	

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
 - ☐ international search (Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (Rule 12.4(a))
 - ☐ international preliminary examination (Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:
 - ☒ the international application as originally filed/furnished
 - ☐ the description:
 - ☐ pages _____ as originally filed/furnished
 - ☐ pages* _____ received by this Authority on _____
 - ☐ pages* _____ received by this Authority on _____
 - ☐ the claims:
 - ☐ pages _____ as originally filed/furnished
 - ☐ pages* _____ as amended (together with any statement) under Article 19
 - ☐ pages* _____ received by this Authority on _____
 - ☐ pages* _____ received by this Authority on _____
 - ☐ the drawings:
 - ☐ pages _____ as originally filed/furnished
 - ☐ pages* _____ received by this Authority on _____
 - ☐ pages* _____ received by this Authority on _____
 - ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.
3. ☐ The amendments have resulted in the cancellation of:
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
 - ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing *(specify)*:
 - ☐ any table(s) related to sequence listing *(specify)*:

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-37

because:

☐ the said international application, or the said claims Nos. 30-37

relate to the following subject matter which does not require an international preliminary examination (*specify*):

The subject matter of claims 30-37 is directed to a method of medical treatment of the human or animal body (Rule 39.1(iv) PCT). No unified criteria exist in the PCT Contracting States for the assessment of the industrial applicability of these claims (Article 33(4) PCT).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 1-37 are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

(see supplemental box)

☐ no international search report has been established for said claims Nos.

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b) and 13ter.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☒ See Supplemental Box for further details.

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims		YES
	Claims	1-37	NO
Inventive step (IS)	Claims		YES
	Claims	1-37	NO
Industrial applicability (IA)	Claims	1-29	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

D1: CA 2406160

D1 discloses the compounds defined in current claims 1-20 and their use in modulating cell proliferation.

D2: CA 2463133

D2 discloses the compounds defined in current claims 1-20 and their use in promoting myelopoiesis.

D3: CA 2473763

D3 discloses certain compounds encompassed by claims 1-11 and 16-20 and their use in modulating cell proliferation.

D4: EP 0335641

D4 discloses certain compounds encompassed by claims 1-20 and their use in non-linear optics.

Observations pertaining to Novelty:

The subject matter of claims 1-37 lack novelty in light of D1.

D1 discloses the same compounds as those defined in current claims 1-20 and thus, the claims directed to compounds (claims 1-20) lack novelty. In addition, D1 discloses the use of these compounds in modulating cell proliferation by modulating tyrosine kinase activity. In particular, D1 discloses the use of these compounds in inhibiting cell proliferation (such as cancer cell proliferation) and in the treatment of cancers such as hematopoietic cell cancers. Furthermore, D1 also discloses the use of these compounds to promote cell proliferation such as promoting myelopoiesis and to treat neutropenia, aplastic anemia and aplasia (see the examples). As a result, the use and method claims (claims 21-37) also lack novelty in light of the disclosure in D1. Therefore, the subject matter of claims 1-37 fails to satisfy Article 33(2) PCT.

The subject matter of claims 1-2 and 30 lack novelty in light of D2.

D2 discloses compounds that are encompassed by current claims 1-20. In addition, D2 discloses the use of these compounds to promote myelopoiesis (and as a result, their use in modulating cell proliferation). As a result, claims 1-22 and 30 lack novelty in light of the disclosure in D2 and therefore, the subject matter of these claims fails to satisfy Article 33(2) PCT.

The subject matter of claims 1-11 and 16-37 lack novelty in light of D3.

D3 discloses compounds that are encompassed by current claims 1-11 and 16-20. In addition, D3 discloses the use of these compounds in modulating cell proliferation by modulating tyrosine kinase activity. As a result, claims 1-11 and 16-37 lack novelty in light of the disclosure in D3 and therefore, the subject matter of these claims fails to satisfy Article 33(2) PCT.

See supplemental box

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

The phrase "selected from" is repeated in claims 7, 9 and 11-18.

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 16-19 lack clarity (Article 6 PCT). The use of the term "optionally" leads to a lack of clarity. It is not evident whether these claims are explicitly defining the 1 to 4 substituents on the phenyl groups or whether those substituents defined in claims 16-19 are only exemplary. In the latter situation, exemplary or preferred embodiments should be defined in separate dependent claims.

Claim 20 does not comply with Rule 6.4(b) PCT. Dependent claim 20 does not include all the limitations of independent claim 1 upon which claim 20 is dependent. In particular, the compounds defined in claim 20 on page 128 (7th compound), page 131 (6th compound), page 134 (10th compound), page 139 (5th, 6th and 7th compounds), page 141 (2nd compound) and page 146 (5th compound) are outside the scope of the compounds defined by Formula I in claim 1. According to the definition given in claim 1, Ar does not include aromatic groups substituted with two substituents that together form a ring. In addition, according to the definition given in claim 1, R³ does not include a polyether or an arylalkoxy group while R⁴ does not include SO₂Ar (claim 1 defines R⁴ as possibly being SO₃Ar).

Claims 22-24 and 30-33 do not comply with Article 6 PCT. Defining the compound as "a compound capable of modulating cell proliferation" (claims 22 and 30), "a compound capable of inhibiting cell proliferation" (claims 23 and 31) and "a compound capable of inhibiting cancer cell proliferation" (claims 24, 32 and 33) fails to define the compounds used in these claims in a clear and explicit manner and forces a person skilled in the art to undertake undue experimentation in order to determine which of the compound encompassed by these claims possess the desired utility. As such, claims 22-24 and 30-33 define the compounds in terms of their desired biological properties rather than in terms of the actual compounds that exhibit these biological properties.

Claims 30-33 lack clarity (Article 6 PCT). The phrase "a cell or animal in need thereof" is indefinite as it does not define the subject matter of these claims in distinct and explicit terms. There is a lack of clarity with respect to what cells or animals are in need of modulation of cell proliferation (claim 30), in need of inhibition of cell proliferation (claim 31), in need of inhibition of cancer cell proliferation (claim 32) and in need of treatment of cancer (claim 33). This is particularly the case for individual cells as it is not evident which cells would exhibit such needs.

General statements in the description which imply that the extent of protection may be expanded in some vague and not precisely defined manner must be removed. The paragraphs on page 6, lines 1-6 and page 123, lines 5-9 imply that the extent of protection may be expanded in a vague and imprecisely defined manner to include the "spirit of the invention" do not comply with Article 6 PCT and should be removed.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Box III

Claims 1-37 relate to an extremely large number of possible compounds, compositions and uses thereof. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found however for only a very small proportion of the defined compounds, compositions and uses thereof. In the present application, the claims so lack support and the specification so lacks disclosure that a meaningful search over the whole of the claimed scope is not possible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts that relate to the compounds defined in claim 20.

It is stressed that the initial phase of the search revealed a very large number of documents that call into question the novelty and inventive step involved in claims 1-20. Only the most relevant of these documents have been cited in the search report. As a result, a meaningful search over the whole of the scope encompassed by claims 1-37 is not possible and the search has been limited as described above.

Continuation of Box V

The subject matter of claims 1-20 lack novelty in light of D4.

D4 discloses a family of compounds defined by a general formula which is at least partially encompassed by the compounds defined in current claims 1-20. As a result, claims 1-20 lack novelty in light of the disclosure in D4 and therefore, the subject matter of these claims fails to satisfy Article 33(2) PCT.

Observations pertaining to Inventive Step:

Given the lack of novelty in claims 1-37 in light of D1-D4 (Article 33(2) PCT), these claims also lack an inventive step in light of D1-D4 in view of Article 33(3) PCT.

Observations pertaining to Industrial Applicability:

The subject matter of claims 1-29 is considered to be industrially applicable and thus fulfills the requirements of Article 33(4) PCT.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

C07C 255/29 (2006.01), *C07C 255/10* (2006.01), *A61P 35/02* (2006.01), *A61P 35/00* (2006.01),
A61K 31/695 (2006.01), *A61K 31/277* (2006.01), *A61K 31/662* (2006.01), *A61K 31/44* (2006.01),
A61K 31/36 (2006.01), *A61K 31/341* (2006.01), *C07C 255/14* (2006.01), *C07C 255/13* (2006.01),
C07C 255/34 (2006.01)